SUPPLEMENTARY METHODS:

MRI tumor volume quantification:

Animals were anesthetized with 1.5%–2% isoflurane (IsoFlo; Abbott) in 100% oxygen. Both cardiac and respiratory gating was applied to minimize motion effects. Acquisition of the magnetic resonance signal was synchronized with the cardiac and respiratory cycles. MRI protocols optimized for assessing pulmonary parenchyma and vessels in normal mice were adapted for operation at 7 Tesla (BioSpec; Bruker BioSpin). Tumor volume quantifications were performed using the 3D-Slicer software as described previously (1). Tumor volumes of some of untreated TL and TD mice have been used from a previous study (2).

Tumor induction in Kras driven mouse models

Kras^{G12D} and Kras^{G12D}; P53^{L/L} mice were maintained in mixed (C57Bl/6, FVB, and S129) background and given adeno virus expressing Cre recombinase (5x10⁶ titer) intranasally at 5 weeks of age for induction of recombination and tumor formation.

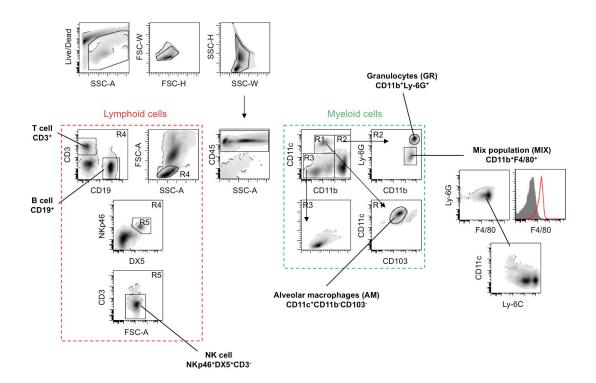
Antibody list for mouse

| Antigen | Clone | Antigen | Clone |
|---------|----------|---------|-----------|
| CD45 | 30-F11 | PD-1 | 29F.1A12 |
| CD3ε | 145-2C11 | Tim-3 | RMT3-23 |
| CD4 | RM4-5 | LAG-3 | 631501 |
| CD8 | 53-6.7 | PD-L1 | 10F.9G2 |
| CD19 | 6D5 | CD25 | PC61 |
| DX5 | DX5 | FasL | MFL3 |
| NKp46 | 29A1.4 | ICOS | C398.4A |
| CD11c | N418 | CXCR3 | CXCR3-173 |
| CD11b | M1/70 | FOXP3 | FJK-16s |
| Ly6G | 1A8 | CTLA-4 | UC10-4B9 |
| Ly6C | HK1.4 | IFNg | XMG1.2 |
| F4/80 | BM8 | IL-2 | JES6-5H4 |
| CD103 | 2E7 | NKG2D | CX5 |
| CD44 | IM7 | DNAM-1 | 10E5 |
| CD62L | MEL-14 | | |

Antibody list for human

| Antigen | Clone | Antigen | Clone |
|---------|--------|---------|-------|
| PD-L1 | 30-F11 | EGFR | AY13 |

Gating method for flow cytometry analysis:



After gating live, single CD45⁺ cells from total lung cells, cells were differentiated into 3 regions: R1, R2, and R3, for identification of myeloid cell populations by CD11c and CD11b. R1 included CD11c⁺CD11b⁻CD103⁻ alveolar macrophages (AM). R2 contained 2 clusters; CD11b⁺Ly-6G⁺ granulocytes (GR) and the other population expressing F4/80. This CD11b⁺F4/80⁺ population was consisted of the different cell types based on Ly-6C and CD11c expression, so they were classified as mixed population (MIX) R3 included lymphoid cells. For lymphoid cell analysis, we used another gating (R4) based on FSC and SSC. R4 contained CD3⁺ (T cell), CD19⁺ (B cell) and DX5⁺NKp46⁺CD3⁻ (NK cell)

SUPPLEMENTARY REFERENCES:

- 1. Chen Z, Cheng K, Walton Z, Wang Y, Ebi H, Shimamura T, et al. A murine lung cancer co-clinical trial identifies genetic modifiers of therapeutic response. Nature. 2012;483:613-7.
- 2. Zhou W, Ercan D, Chen L, Yun CH, Li D, Capelletti M, et al. Novel mutant-selective EGFR kinase inhibitors against EGFR T790M. Nature. 2009;462:1070-4.